REMARKS

This invention provides for, *inter alia*, a process for transdermally administering a therapeutic compound having a low skin penetration rate using a device for transdermal therapeutic therapy, such as a transdermal therapeutic device ("TTS"), by applying ultrasound only during an initial phase once the device is attached to the skin. Applicants discovered that when the inventive process is used the device continues to administer the compound long after ultrasound has been terminated and that one does not have to apply ultrasound continuously in order to administer the compound; this time period for administration lasts for periods of time up to, for example, 7 days. This invention also provides for a device that administers the therapeutic compound in accordance with the process.

It is believed that no fee is required for the consideration of this Amendment by the Examiner. However, should a fee be required, the Director is authorized to charge such fee to Deposit Account 50-0320.

Claims 1 to 18 and 50, which have been withdrawn by the Examiner as being drawn to a non-elected invention, are cancelled without prejudice or the intention of creating estoppel as these claims, if elected, are non-statutory and hence would have been rejected under 35 USC §§ 101 and 112, second paragraph. Applicants reserve the right to file a divisional application directed to this subjected matter once the claims are drafted in conventional US format.

The amendment to claim 19 makes the rejection of this claim under 35 USC § 112, second paragraph, moot and its withdrawal is requested. As this change does not affect the scope of the claim (i.e. narrow the claim) and is directed formal matters, the application of the doctrine of equivalents is not affected.

Applicants note that the Restriction Requirement has been maintained. Applicants continue to urge that the Requirement is not proper for reasons of record and request its modification or withdrawal.

Applicants further amended claim 19 to emphasized that only ultrasound and not some other method of improving the penetrability of the active compound through the skin, e.g., iontophoresis, is employed. Support for this language resides in the fact that the instant invention only uses ultrasound; see, for example, the discussion on page 5, line 14 to page 5, line 5, page 9 lines 5 to 23 (e.g., "as a consequence of ultrasonic treatment") and the example on pages 12 and 13, wherein only ultrasound is employed and not ultrasound in connection with some other method of enhancing penetrability, such as iontophoresis.

Applicants further amended claims 25 to 27, 29 and 30 to delete phrases such as "particularly" or "particularly preferably" in order to place the claims in compliance with conventional U.S. practice. Again, as these changes do not narrow the scope of the claims, the application of the doctrine of equivalents is not affected.

Applicants further added claims 51 and 52. These claims are directed to some preferred embodiments, which may be found on pages 11 and 12 of the specification.

Claim 19 stands rejected under 35 USC § 102(e) for allegedly being anticipated by Henley. Applicants respectfully disagree and urged that Henley does not meet each and every element of the invention as claimed. First, Henley does not use ultrasound by itself; rather Henley employs ultrasound in connection with an electrical stimulus ("iontophoretic-ultrasonic" device). Second, Henley does not meet the element of wearing the patch during the long-term phase without further treatment of the patch with ultrasound. Accordingly, withdrawal of this rejection is requested.

The inventive process, as claimed, is directed to a process for "treating the skin-adherent patch with ultrasound during the initial phase" and "wearing the patch during a subsequent long-term phase without additional treatment." Applicants urge that Henley does not meet these claim elements.

Henley is directed to a device and method that employs a "iontophoretic or iontophoretic-ultrasonic (ionosonic) transdermal delivery of medication across the skin or other biological membrane" (see Abstract). With this process the patient experiences is a "mild tingling sensation or other such stimulation" (see, e.g., col. 6 lines 37-57). As discussed in the paragraph bridging pages 2 and 3 of the specification, this effect is something the present invention avoids. Hence, as Henley does not solely use ultrasound, the publication cannot anticipate claims 19.

Moreover, Henley does not provide any teaching that the active compound will continue to be administered to the patient once the iontophoretic or iontophoretic-ultrasonic source has been removed. As indicated in column 6, line 58 to column 7, line 38, an advantage of that device is that it is programmable, thereby permitting one to control the absorption of the active into the dermal and subdermal layers, while minimizing the systemic absorption. Hence, Henley does not teach a process which involves "wearing the patch during a subsequent long-term phase without additional ultrasonic treatment." Hence, Henley does not meet this second claim element.

Thus, in view of the foregoing, it is respectfully urged that Henley does not teach each and every element of the invention as claimed and withdrawal of this rejection is requested.

Claims 20 to 37 stand rejected under 35 USC § 103(a) for allegedly being unpatentable over Henley in view of Rowe *et al.*, US 6,234,990 B1 ("Rowe"), Kost *et al.*, US 4,948,587 ("Kost I"), Kost *et al.*, US 4,767,402 ("Kost II"), and Kost *et al.*, US 6,041,253 (Kost III).

Applicants respectfully disagree since none of these prior publications taken in any fair combination suggests inventive process wherein after the patch is treated with ultrasound for a short period of time, the compound will continue to administer the active compound over a long period of time. Further, these prior publications do not suggest that this may be accomplished with active compounds that are difficult to administrate transdermally because they have a low penetration rate. Accordingly, reconsideration and withdrawal of this rejection is requested.

As discussed above, the inventive process, as claimed, is directed to a process for administering active compounds that have a low skin penetration rate. This process includes the steps of "treating the skin-adherent patch with ultrasound during the initial phase" and "wearing the patch during a subsequent long-term phase without additional treatment." As discussed on page 11, with just one ultrasound treatment, the device transdermally administers active agents, which have low penetration rates, for a time period that can last up to, for example, seven days. In order words, in the inventive process, the active compounds are delivered onto and through the skin the skin without additional ultrasonic treatment (see first paragraph on page 5). Applicants urge that Henley taken in any fair combination does not suggest this method.

Henley is directed to a device and method that employs the "iontophoretic or iontophoretic-ultrasonic (ionosonic) transdermal delivery of medication across the skin or other biological membrane" (see Abstract). Further, Henley does not provide any teaching that the active compound will continue to be administered to the patient once the iontophoretic or iontophoretic-ultrasonic source has been removed. Hence, Henley differs from the present process in at least two significant aspects. Applicants respectfully urge that the remaining prior publications do not correct for these deficiencies.

First, it is respectfully urged that combining the teaching of a publication directed to a iontophoretic or iontophoretic-ultrasonic delivery system with a publication directed to an ultrasonic delivery system is improper because the systems involve different technology. As discussed above, iontophoretic or iontophoretic-ultrasonic delivery systems use electric current, something the inventive process seeks to avoid. Hence, one would not look to Henley if he or she was interested in a process that uses only ultrasound. Similarly, Kost I is not properly combined since the publication provides for transbuccal drug delivery system, a delivery system that is different from transdermal systems.

Second, even if the combination were proper, a point that Applicants do not concede, the rejection would still not establish a *prima facie* case of obviousness. As previously noted, a feature of the present process is the discovery that the patch continues to deliver an active agent, which can have a low penetration rate, for a long period of time after the removal of ultrasonic source, without the need for further treatment. None of the prior publications relied on the rejection suggests this. In fact, Henley teaches just the opposite and relies upon a computer program to deliver the electrical current to keep the concentration of the active agent in the dermis and subdermis at the correct levels. Hence, Henley teaches away from the present invention.

Finally, none of the prior publications relied upon in the rejection suggests that one may administer an active compound that has a low skin penetration rate for a long time period with just a short initial ultrasonic treatment. Applicants urge that based upon the teachings relied upon in the rejection, this observation is indeed surprising since, taken together, the prior publications would suggest that one would have to reapply the ultrasonic treatment.

Thus, in view of the foregoing, it is urged that Henley does not teach the present invention and its withdrawal it respectfully requested.

Favorable action is earnestly solicited.

Respectfully submitted,

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